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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/935,100	08/22/2001	David B. Weiner	UPN-4099	2243

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EXAMINER	
PARKIN, JEFFREY S	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 04/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/935,100	WEINER ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

HC

Response to Amendment

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the amendment filed 03 January, 2005. Claim 32 was amended and new claims 35-46 introduced. Claims 32-46 are currently under examination.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The previous rejection of claim 32 under 35 U.S.C. § 102(b) as being clearly anticipated by Sato *et al.* (1990), is hereby withdrawn in response to applicants' amendment and arguments.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Newly submitted claims 36, 39, 40, 42, 43, 45, and 46 are

rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). The claims have been amended to recite antibodies that bind to **amino acid 2-12 of Vpr**, as well as, **humanized** monoclonal antibodies. Concerning the binding specificity of any given antibody, the disclosure (see p. 87) only notes that epitopes have been identified between amino acids **2-21** and **9-20.** There is nothing in the specification that supports these claim limitations. Concerning the nature of the antibody, nothing in the disclosure describes the preparation of humanized monoclonal antibodies to Vpr. While the disclosure discusses Vpr-specific monoclonals, it does **not** disclose the isolation and characterization of a single **human** monoclonal antibody that binds to Vpr. According, the skilled artisan would reasonably conclude that applicants were not in possession of the claimed invention at the time of filing.

Claims 32-46 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed toward a method of treating individuals exposed to or infected with HIV by administering anti-Vpr antibodies. The claims are directed toward pharmaceutical compositions comprising anti-Vpr monoclonal antibodies, pharmaceutical compositions comprising anti-Vpr antibodies that inhibit Vpr

enhancement of HIV replication, and methods of treating individuals exposed to HIV by administering said pharmaceutical compositions. The disclosure (see p. 65) clearly states that "anti-vpr antibodies may be administered as **therapeutics** to **treat individuals infected** with HIV. The anti-vpr [sic-Vpr] antibodies are preferably produced against eukaryotically-produced vpr [sic-Vpr]. They are administered in an effective dose; i.e. a dose sufficient to inactivate some or all of the vpr [sic-Vpr] present in the individual such that the progress of HIV in the individual is inhibited or otherwise reduced. Multiple doses may be administered." Thus, to practice the claimed invention, the skilled artisan would require a composition comprising a high-affinity antibody or antibodies with the desired pharmacological profile.

As previously set forth, the legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

Inadequate Direction/Guidance Provided

The disclosure fails to provide adequate guidance pertaining to the structural and functional characteristics of the anti-Vpr antibodies present in the pharmaceutical composition. **The specification is silent pertaining to the epitope(s) recognized, the affinity of the antibody composition, the avidity of the antibody composition, and the pharmacological properties (i.e., serum half-life, bioavailability, clearance rate, sequestration by serum proteins, target distribution, target levels, etc.).** The skilled artisan would require a knowledge of these various properties before attempting to administer the antibody composition to a patient. Moreover, Vpr is a regulatory protein that is not readily accessible to circulating antibodies. Thus, even if applicants were able to identify a high-affinity antibody, it is not readily manifest that said antibody would have the requisite neutralizing activity to be effective as a therapeutic.

Claim Breadth is Excessive

The claims are broadly directed toward any population of anti-Vpr antibodies. Thus, they may include specific monoclonal reagents (none of which are described in the specification), polyclonal reagents, or recombinant antibodies. The claims do not specify any type of neutralizing activity or other properties for the antibodies. In order to practice the claimed invention the skilled artisan would need a purified, well-characterized reagent (i.e., a Mab produced from a specific hybridoma). However, the specification is silent pertaining the properties of any given antibody composition.

State-of-the-Art

The state-of-the-art vis-à-vis the treatment of HIV infection using immunotherapeutics can be characterized by unpredictability and frequent failure. This is not surprising since the correlates of protective immunity remain to be

elucidated (Burton and Moore, 1998; Feinberg and Moore, 2002; Moore and Burton, 1999; Johnston, 2000; Letvin, 1998). Thus, the skilled artisan, even if armed with a highly specific neutralizing reagent, cannot predict if that reagent will have a meaningful clinical effect. Each antibody composition must be tested empirically, preferably in a human host since most animal models are inadequate and do not allow the direct extrapolation of findings from one system to another. Moreover, some passive immunotherapy studies have reported that there was no clinical benefit in HIV-infected patients receiving Ig preparations (Jacobson *et al.*, 1993). This is not surprising considering all the uncertainty associated with attempting to identify the correlates of protective immunity and the ability of the virus to direct the immune response predominantly toward low affinity antibody responses (Kohler et al., 1992).

Absence of Working Embodiments

The disclosure fails to provide any working embodiments demonstrating the HIV-1 or -2 Vpr-specific antisera are effective at combatting HIV infection. Considering the unpredictability of the art and nature of the invention, the skilled artisan would clearly require suitable working examples before contemplating practicing the invention on an infected patient.

When all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation to practice the claimed invention.

Response to Arguments

Applicants' traverse and submit that the invention is fully enabled. However, applicants' response failed to provide any objective scientific data that addresses the concerns set forth *supra*. In the absence of such a showing, the rejection is proper.

Finality of Office Action

Applicants' amendment necessitated any and all new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). **A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.**

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Formal communications may be submitted through the official facsimile number which is (703) 872-9306. Hand-carried formal communications should be directed toward the customer window located in Crystal Plaza Two, 2011 South Clark Place, Arlington, VA. Applicants are directed toward the O.G. Notice for further guidance. 1280 O.G. 681. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval

(PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

01 April, 2005